

ABSTRACT

The present invention is related to enhancing the function of anti-tumor antibodies by regulating FcγRIIB-mediated activity. In particular, disrupting SHIP activation by FcγRIIB enhances cytotoxicity elicited by a therapeutic antibody *in vivo* in a human. The invention further provides an antibody, *e.g.*, an anti-tumor antibody, with a variant Fc region that results in binding of the antibody to FcγRIIB with reduced affinity. A variety of transgenic mouse models demonstrate that the inhibiting FcγRIIB molecule is a potent regulator of cytotoxicity *in vivo*.